

In the Claims:

Cancel Claims 1 – 36, and add claims 37 – 100 attached herewith. Claim 37 – 100 correspond to Claims 1 – 64 of PCT Application No. IL99/00444.

37. (NEW) A method of expanding a population of cells, while at the same time inhibiting differentiation of the cells, the method comprising the step of providing the cells with conditions for cell proliferation and, at the same time, for reducing a capacity of said cells in utilizing copper.

38. (NEW) The method of claim 37, wherein the cells are *in-vivo*, where said conditions for cell proliferation are naturally provided, whereas reducing said capacity of the cells in utilizing transition metals is effected by administering a transition metal chelator which binds copper.

39. (NEW) The method of claim 38, wherein reducing said capacity of the cells in utilizing copper is further effected by administering Zinc.

40. (NEW) The method of claim 37, wherein the cells are *in-vivo*, where said conditions for cell proliferation are naturally provided, whereas reducing said capacity of the cells in utilizing copper is effected by administering Zinc.

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42. (NEW) The method of claim 37, wherein reducing said capacity of the cells in utilizing copper is effected by a transition metal chelator that binds copper.

44. (NEW) The method of claim 37, wherein the cells are *ex-vivo*.

45. (NEW) The method of claim 44, wherein providing the cells with said conditions for cell proliferation include providing the cells with nutrients and with cytokines.

46. (NEW) The method of claim 45, wherein said cytokines are early acting cytokines.

47. (NEW) The method of claim 46, wherein said early acting cytokines are selected from the group consisting of stem cell factor, FLT3 ligand, interleukin-6, thrombopoietin and interleukin-3.

48. (NEW) The method of claim 45, wherein said cytokines are late acting cytokines.

49. (NEW) The method of claim 48, wherein said late acting cytokines are selected from the group consisting of granulocyte colony stimulating factor, granulocyte/macrophage colony stimulating factor and erythropoietin.

50. (NEW) The method of claim 44, wherein said cells are selected from the group consisting of hematopoietic cells, neural cells and oligodendrocyte cells, skin cells, hepatic cells, embryonal stem cells, plant cells, muscle cells, bone cells, mesenchymal cells, pancreatic cells, chondrocytes and stroma cells.

51. (NEW) The method of claim 50, wherein said cells are derived from a source selected from the group consisting of bone marrow, peripheral blood and neonatal umbilical cord blood.

52. (NEW) The method of claim 50, wherein said cells are enriched for hematopoietic CD₃₄⁺ cells.

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FOOTNOTES

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53. (NEW) The method of claim 37, wherein said cells are selected from the group consisting of non-differentiated stem cells and committed progenitor cells.

54. (NEW) A method of hematopoietic cells transplantation comprising the steps of:

(a) obtaining hematopoietic cells to be transplanted from a donor;

(b) providing said cells *ex-vivo* with conditions for cell proliferation and, at the same time, for reducing a capacity of said cells in utilizing cooper, thereby expanding a population of said cells, while at the same time, inhibiting differentiation of said cells; and

(c) transplanting said cells to a patient.

55. (NEW) The method of claim 54, wherein said donor and said patient are a single individual.

56. (NEW) The method of claim 54, wherein obtaining said hematopoietic cells is from a source selected from the group consisting of peripheral blood, bone marrow, neonatal umbilical cord blood and embryonal stem cells.

57. (NEW) The method of claim 56, wherein obtaining said hematopoietic cells further includes enriching said cells for stem cells.

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58. (NEW) The method of claim 56, wherein obtaining said hematopoietic cells further includes enriching said cells for progenitor cells.

59. (NEW) A method of genetically modifying stem cells with an exogene comprising the steps of:

- (a) obtaining stem cells to be genetically modified;
- (b) providing said cells *ex-vivo* with conditions for cell proliferation and, at the same time, for reducing a capacity of said cells in utilizing cooper, thereby expanding a population of said cells, while at the same time, inhibiting differentiation of said cells; and
- (c) genetically modifying said cells with the exogene.

60. (NEW) The method of claim 59, wherein genetically modifying is effected by a vector including the exogene.

61. (NEW) A method of adoptive immunotherapy comprising the steps of:

- (a) obtaining progenitor hematopoietic cells from a patient;
- (b) providing said cells *ex-vivo* with conditions for cell proliferation and, at the same time, for reducing a capacity of said cells in utilizing cooper, thereby expanding a population of said cells, while at the same time, inhibiting differentiation of said cells; and
- (c) transplanting said cells to the patient.

62. (NEW) A method of mobilization of bone marrow stem cells into the peripheral blood of a donor for harvesting the cells comprising the step of:

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66. (NEW) A method of decelerating maturation/differentiation of erythroid precursor cells for the treatment of β -hemoglobinopathic patients comprising the step of administering to the patient an agent for reducing a capacity of said cells in utilizing cooper, thereby expanding a population of stem cells, while at the same time, inhibiting differentiation of said stem cells, such that upon natural removal of said agent from the body, the stem cells undergo accelerated maturation resulting in elevated production of fetal hemoglobin.

67. (NEW) The method of claim 66, wherein said agent is selected from the group consisting of a transition metal chelator and Zinc.

68. (NEW) A therapeutical *ex-vivo* cultured cell preparation comprising *ex-vivo* cells propagated in the presence of an agent, said agent reducing a capacity of said cells in utilizing copper, thereby expanding a population of said cells, while at the same time, inhibiting differentiation of said cells.

69. (NEW) The method of claim 68, wherein said agent is selected from the group consisting of a transition metal chelator which binds copper, and Zinc.

70. (NEW) A method of preservation of stem cells comprising the step of handling the stem cell in at least one of the steps selected from the group consisting of harvest, isolation and storage, in a presence of a transition metal chelator which binds copper and/or Zinc.

71. (NEW) Stem cell collection bags, separation and washing buffers supplemented with an effective amount or concentration of a transition metal chelator which binds copper and/or with Zinc, which inhibits cell differentiation.

72. (NEW) An assay of determining whether a transition metal chelator which binds copper causes inhibition or induction of differentiation, the assay comprising the step of culturing a population of stem or progenitor cells or cells of a substantially non-differentiated cell line, in the presence of the transition metal chelator and monitoring differentiation of said cells, wherein if differentiation is

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increased as is compared to non-treated cells, the transition metal chelator induces differentiation, whereas if differentiation is decreased or as compared to non-treated cells, or if differentiation is absent altogether, the transition metal chelator inhibits differentiation.

73. (NEW) An assay of determining whether a transition metal chelator which binds copper causes inhibition or induction of differentiation, the assay comprising the step of culturing a population of cells in the presence of the transition metal chelator and monitoring copper content of said cells, wherein if the copper content of said cells is increased as is compared to non-treated cells, the transition metal chelator induces differentiation, whereas if copper content is decreased as compared to non-treated cells the transition metal chelator inhibits differentiation.

74. (NEW) A method of inducing differentiation in a population of cells, the method comprising the step of providing the cells with a transition metal chelator which binds copper and which is effective in inducing cell differentiation.

75. (NEW) The method of claim 74, wherein the cells are *in-vivo*.

76. (NEW) The method of claim 74, wherein the cells are grown *ex-vivo*.

77. (NEW) The method of claim 74, wherein the cells are hematopoietic cells.

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79. (NEW) The method of claim 74, wherein said transition metal chelator is a tripeptide.

81. (NEW) The method of claim 74, wherein said transition metal chelator is GGH.

82. (NEW) The method of claim 74, wherein said transition metal chelator is a peptide or a peptide analog.

83. (NEW) The method of claim 74, wherein said transition metal chelator includes a peptide sequence.

84. (NEW) The method of claim 83, wherein said peptide sequence is selected from the group consisting of SEQ ID NOs:1 and 2.

85. (NEW) The method of claim 74, wherein said cells are selected from the group consisting of hematopoietic stem or progenitor cells, neural stem or progenitor cells, oligodendrocyte stem or progenitor cells, skin stem or progenitor

cells, hepatic stem or progenitor cells, muscle stem or progenitor cells, bone stem or progenitor cells, mesenchymal stem or progenitor cells, pancreatic stem or progenitor cells, stem or progenitor chondrocytes, stroma stem or progenitor cells, embryonal stem cells and cultured expanded stem or progenitor cells.

86. (NEW) The method of claim 74, wherein said cells are derived from a source selected from the group consisting of bone marrow, peripheral blood and neonatal umbilical cord blood.

87. (NEW) The method of claim 74, wherein said cells are enriched for hematopoietic CD₃₄⁺ cells.

88. (NEW) The method of claim 74, wherein said cells are selected from the group consisting of non-differentiated stem cells and committed progenitor cells.

89. (NEW) A method of inducing terminal differentiation in acute leukemic cells, the method comprising the step of providing the cells with a transition metal chelator which binds copper and which is effective in inducing cell differentiation.

90. (NEW) The method of claim 89, wherein said cells are selected from the group consisting of *in-vivo* and *ex-vivo* cells.

91. (NEW) A method of induction of differentiation of non-leukemic hematopoietic progenitor cells, the method comprising the step of providing the cells

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with a transition metal chelator which binds copper and which is effective in inducing cell differentiation.

92. (NEW) The method of claim 91, wherein said cells are selected from the group consisting of *in-vivo* and *ex-vivo* cells.

93. (NEW) A method of *ex-vivo* differentiation of normal stem cells into lineage committed progenitor cells, the method comprising the step of providing the cells with a transition metal chelator which binds copper and which is effective in inducing cell differentiation.

94. (NEW) A method of *ex-vivo* differentiation of stem cells into dendritic cell committed progenitors, the method comprising the step of providing the cells with a transition metal chelator which binds copper and which is effective in inducing cell differentiation.

95. (NEW) A pharmaceutical composition for inducing differentiation in a population of cells, comprising transition metal chelator which binds copper and which is effective in inducing cell differentiation, and a pharmaceutically acceptable carrier.

96. (NEW) The composition of claim 95, wherein said transition metal chelator is a tripeptide.

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97. (NEW) The composition of claim 95, wherein said transition metal chelator is selected from the group consisting of GGH, GHL and 1,4,8,11-tetraaza cyclotetradecane.

98. (NEW) The composition of claim 95, wherein said transition metal chelator is GGH.

99. (NEW) The composition of claim 95, wherein said transition metal chelator is a peptide or a peptide analog.

100. (NEW) The composition of claim 95, wherein said transition metal chelator includes a peptide sequence.

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